```
      ---  -----  -----------
? s hepatoma or sarcoma
           51342  HEPATOMA
          154598  SARCOMA
      S1  204902  HEPATOMA OR SARCOMA
? s arginin?
      S2  211705  ARGININ?
? s s1 and s2
          204902  S1
          211705  S2
      S3     955  S1 AND S2
? s arginine(5n)deiminase
          206952  ARGININE
            1641  DEIMINASE
      S4    1050  ARGININE(5N)DEIMINASE
? s s1 and s4
          204902  S1
            1050  S4
      S5      21  S1 AND S4
? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
      S6      14  RD  (unique items)
? t s6/3,k,ab/1-14

 6/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14960182   PMID: 15187998
    Induction  of  hyperammonia  in  irradiated  hepatoma  cells:  a
recapitulation and possible explanation of the phenomenon.
  van  Rijn  J;  van  den  Berg  J;  Schipper  R  G; de Jong S; Cuijpers V;
Verhofstad A A J; Teerlink T
  Radiation  Oncology,  VU  University Medical Center, PO Box 7057, 1007 MB
Amsterdam, The Netherlands. j.vanrijn@vumc.nl
  British journal of cancer (England)   Jul 5 2004,  91  (1)  p150-2,
ISSN 0007-0920--Print   Journal Code: 0370635
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed

    Induction  of  hyperammonia  in  irradiated  hepatoma  cells:  a
recapitulation and possible explanation of the phenomenon.
  Enzyme  No.:  EC  3.     (Hydrolases);  EC  3.5.3.6    (  ***arginine***
deiminase)
  Chemical  Name:  Culture  Media;  Arginine;  Ammonia;  Hydrolases;
arginine deiminase


 6/3,K,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

10625601   PMID: 7591961
   Anti-tumor  activity  of  arginine deiminase from Mycoplasma
argini and its growth-inhibitory mechanism.
  Takaku H; Matsumoto M; Misawa S; Miyazaki K
  Pharmaceuticals  and  Biotechnology Laboratory, Japan Energy Corporation,
```

Saitama.
Japanese journal of cancer research - Gann (JAPAN) Sep 1995, 86 (9) p840-6, ISSN 0910-5050--Print Journal Code: 8509412
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Two kinds of ***arginine*** ***deiminase*** (AD, EC 3.5.3.6) were purified from cell extracts of Mycoplasma arginini (a-AD) and Mycoplasma hominis (h-AD), and their enzymic properties and anti-tumor activities were compared. The a-AD enzyme strongly inhibited the growth of mouse hepatoma cell line MH134 in vitro, and its concentration required for 50% growth inhibition (IC50) was estimated to be about 10 ng/ml. The IC50 value of h-AD against the same cell line was estimated to be about 100 ng/ml, due to its low enzyme activity under the physiological pH condition, i.e., pH 7.4. These results show that the reaction pH profile of the a-AD was superior to that of the h-AD as an anti-tumor enzyme. Moreover, the effects of L-arginine metabolism-related substances on the anti-tumor activity of the a-AD were examined to study the growth-inhibitory mechanism of this enzyme. The addition of 2 or 4 mM L-arginine restored, in a dose-dependent manner, the growth of mouse MH134 hepatoma and Meth A fibrosarcoma cell lines that had been inhibited by 20 ng/ml of the a-AD. The addition of 2 or 4 mM L-ornithine, which is biosynthesized from L-arginine in the urea cycle and is the starting material in the polyamine-biosynthesis pathway, also partially restored it in a dose-dependent manner. These results indicate that the tumor cell growth inhibition caused by a-AD originates from the depletion of the essential nutrient L-arginine, and that the resulting block of the polyamine-biosynthesis pathway is involved in part in the inhibitory mechanism.

Anti-tumor activity of arginine deiminase from Mycoplasma argini and its growth-inhibitory mechanism.

Two kinds of ***arginine*** ***deiminase*** (AD, EC 3.5.3.6) were purified from cell extracts of Mycoplasma arginini (a...

... anti-tumor activities were compared. The a-AD enzyme strongly inhibited the growth of mouse hepatoma cell line MH134 in vitro, and its concentration required for 50% growth inhibition (IC50) was...

... 4 mM L-arginine restored, in a dose-dependent manner, the growth of mouse MH134 hepatoma and Meth A fibrosarcoma cell lines that had been inhibited by 20 ng/ml of...

Enzyme No.: EC 3. (Hydrolases); EC 3.5.3.6 (***arginine*** deiminase)
Chemical Name: Antineoplastic Agents; Sodium Dodecyl Sulfate; Arginine; Hydrolases; arginine deiminase

6/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10155972 PMID: 7765234
High-level expression of Mycoplasma arginine deiminase in Escherichia coli and its efficient renaturation as an anti-tumor enzyme.
Misawa S; Aoshima M; Takaku H; Matsumoto M; Hayashi H
Pharmaceuticals and Biotechnology Laboratory, Japan Energy Corporation, Saitama.
Journal of biotechnology (NETHERLANDS) Aug 15 1994, 36 (2) p145-55, ISSN 0168-1656--Print Journal Code: 8411927
Publishing Model Print

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The arginine deiminase (AD) gene was cloned from Mycoplasma arginini and expressed in the cytosol of Escherichia coli as inclusion bodies with an expression level of at least 20% of the total bacterial proteins. The inclusion bodies were solubilized with 6 M guanidine hydrochloride (Gdn-HCl) under reducing conditions, in order to avoid incorrect disulfide-bond formation of the recombinant (r-) AD molecules, and renaturation was performed under various refolding conditions. The optimum renaturation conditions were found to be incubation for 90 h at pH 7.5 and 15 degrees C. The resulting completely refolded r-AD was purified to homogeneity by anion-exchange and arginine-affinity chromatography and its activity yield was 72.5%. The specific activity of the purified r-AD was comparable to and its amino acid composition was identical to those of Mycoplasma AD, and NH2-terminal sequence analysis revealed that its methionine residue corresponding to the translation initiation codon had been removed completely. Anti-tumor activity analyses showed that r-AD inhibited the growth of two mouse cell lines, hepatoma MH134 and fibrosarcoma Meth A, strongly in vitro at concentrations in excess of 10 ng ml-1. Moreover, when MH134-implanted mice were given single intravenous injections of r-AD at doses of 50 mg kg-1 and higher, their survival times were prolonged significantly. These results, taken together, indicate that the enzymatic properties and biological actions of r-AD were highly consistent with those of Mycoplasma AD.

High-level expression of Mycoplasma arginine deiminase in Escherichia coli and its efficient renaturation as an anti-tumor enzyme.

The arginine deiminase (AD) gene was cloned from Mycoplasma arginini and expressed in the cytosol of Escherichia coli...

... tumor activity analyses showed that r-AD inhibited the growth of two mouse cell lines, hepatoma MH134 and fibrosarcoma Meth A, strongly in vitro at concentrations in excess of 10 ng...

Enzyme No.: EC 3. (Hydrolases); EC 3.5.3.6 (***arginine*** deiminase)

Chemical Name: Antineoplastic Agents; DNA, Bacterial; Hydrolases; arginine deiminase

6/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09882623 PMID: 8276724

Chemical modification by polyethylene glycol of the anti-tumor enzyme ***arginine*** ***deiminase*** from Mycoplasma arginini.

Takaku H; Misawa S; Hayashi H; Miyazaki K

Pharmaceuticals and Biotechnology Laboratory, Nikko Kyodo Co., Ltd., Saitama.

Japanese journal of cancer research - Gann (JAPAN) Nov 1993, 84 (11) p1195-200, ISSN 0910-5050--Print Journal Code: 8509412

Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Amino acid-degrading enzymes are known to inhibit the growth of tumor cells in culture by depleting amino acids in the medium. Here we demonstrate that ***arginine*** ***deiminase*** (EC 3.5.3.6) from Mycoplasma arginini had stronger growth-inhibitory activity against all 4 kinds of tumor cell lines tested than L-asparaginase and arginase, which

are well-known anti-tumor enzymes. Next, chemical modification of the arginine deiminase molecule with polyethylene glycol was shown to enhance its potency as an anti-tumor enzyme. The percentage of modified amino groups per molecule was estimated to be 51% of the total amino groups, and the average molecular weight was estimated to be about 400,000 by gel-filtration HPLC. The enzymic activity of the modified enzyme was 25.5 units/mg protein, which was equivalent to 57% of that of the native enzyme. The modified enzyme strongly inhibited growth of a mouse hepatoma cell line, MH134, at a concentration of more than 10 ng/ml, showing almost the same dose-response curve as the native enzyme. When a bolus of 5 units of the modified enzyme was intravenously injected into male BDF1 mice, L-arginine in the blood completely disappeared within 5 min, and remained undetectable for more than 8 days. On the other hand, in the case of bolus injection of the same number of units of native enzyme, the plasma L-arginine level recovered up to 66% of the control level at 8 days. These results suggest that this modified enzyme has a longer plasma clearance time and may be more effective as a new anti-tumor agent than the native enzyme.

Chemical modification by polyethylene glycol of the anti-tumor enzyme ***arginine*** ***deiminase*** from Mycoplasma arginini.

...tumor cells in culture by depleting amino acids in the medium. Here we demonstrate that ***arginine*** ***deiminase*** (EC 3.5.3.6) from Mycoplasma arginini had stronger growth-inhibitory activity against all... ... asparaginase and arginase, which are well-known anti-tumor enzymes. Next, chemical modification of the arginine deiminase molecule with polyethylene glycol was shown to enhance its potency as an anti-tumor enzyme...

... of that of the native enzyme. The modified enzyme strongly inhibited growth of a mouse hepatoma cell line, MH134, at a concentration of more than 10 ng/ml, showing almost the...

...Enzyme No.: 5.1.1 (Asparaginase); EC 3.5.3.1 (Arginase); EC 3.5.3.6 (***arginine*** ***deiminase***)

Chemical Name: Growth Inhibitors; Polyethylene Glycols; Citrulline; Arginine; Hydrolases; Asparaginase; Arginase; arginine deiminase

6/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12/11/06

09209249 PMID: 1568792

In vivo anti-tumor activity of arginine deiminase purified from Mycoplasma arginini.

Takaku H; Takase M; Abe S; Hayashi H; Miyazaki K
Department of Pharmaceuticals, Nippon Mining Company, Saitama, Japan.

International journal of cancer. Journal international du cancer (UNITED STATES) May 8 1992, 51 (2) p244-9, ISSN 0020-7136--Print
Journal Code: 0042124
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Arginine ***deiminase*** (EC 3.5.3.6) was purified to homogeneity from the cell extract of Mycoplasma arginini by molecular-sieve, anion-exchange and arginine-affinity chromatographies. The purified enzyme was composed of 2 identical sub-units with a molecular weight of 45.000 and had a pI of 4.7. Its Vmax value and Km value for L-arginine were estimated to be 50 units/mg protein and 0.2 mM, respectively. It exerted maximal enzyme activity at pH 6.0-7.5 and at 50 degrees C. The ***arginine***

deiminase was stable at neutral pH. When injected i.v. into mice, the half-life of the ***arginine*** ***deiminase*** in blood was about 4 hr. In culture, the enzyme strongly inhibited the growth of 6 kinds of mouse tumor cell lines by depleting L-arginine in the culture media. When the in vivo growth-inhibitory activity of arginine deiminase was tested for the 6 tumor cell lines, i.p. administration of the purified enzyme effectively prolonged the survival time of the mice injected with all kinds of the tumor cell lines. Especially, the in vivo growth of a ***hepatoma*** cell line, MH134, was completely prevented by the daily administration at a dose of 0.2 mg/mouse for 14 days. These results raise the possibility of the use of the arginine deiminase derived from Mycoplasma arginini as a new anti-tumor drug.

In vivo anti-tumor activity of arginine deiminase purified from Mycoplasma arginini.

Arginine ***deiminase*** (EC 3.5.3.6) was purified to homogeneity from the cell extract of Mycoplasma...

...maximal enzyme activity at pH 6.0-7.5 and at 50 degrees C. The ***arginine*** ***deiminase*** was stable at neutral pH. When injected i.v. into mice, the half-life of the arginine deiminase in blood was about 4 hr. In culture, the enzyme strongly inhibited the growth of...
... depleting L-arginine in the culture media. When the in vivo growth-inhibitory activity of arginine deiminase was tested for the 6 tumor cell lines, i.p. administration of the purified enzyme...

... with all kinds of the tumor cell lines. Especially, the in vivo growth of a hepatoma cell line, MH134, was completely prevented by the daily administration at a dose of 0...

... mg/mouse for 14 days. These results raise the possibility of the use of the arginine deiminase derived from Mycoplasma arginini as a new anti-tumor drug.

...; therapy--DT; Melanoma, Experimental--drug therapy--DT; Mice; Mycoplasma--enzymology--EN; Pseudomonas putida--enzymology--EN; Sarcoma%% 180--drug therapy--DT; Tumor Cells, Cultured

*** Enzyme No.: EC 3. (Hydrolases); EC 3.5.3.6 (*** arginine ******
deiminase)

Chemical Name: Hydrolases; arginine deiminase

6/3,K,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12/11/06

08507797 PMID: 2164440

Potent growth inhibition of human tumor cells in culture by arginine deiminase purified from a culture medium of a Mycoplasma-infected cell line.

Miyazaki K; Takaku H; Umeda M; Fujita T; Huang W D; Kimura T; Yamashita J ; Horio T

Kihara Institute for Biological Research, Yokohama City University, Japan.

Cancer research (UNITED STATES) Aug 1 1990, 50 (15) p4522-7, ISSN 0008-5472--Print Journal Code: 2984705R

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Two kinds of growth-inhibitory substances were found in culture of a Rous ***sarcoma*** virus-transformed rat liver cell line, RSV-BRL. The two

substances were purified from the serum-free culture medium and identified as transforming growth factor beta 1 and Mycoplasma-derived arginine ***deiminase*** (EC 3.5.3.6), respectively. The ***arginine*** deiminase was an acid-labile but dithiothreitol-resistant protein with a molecular weight of 45,000 and pI 4.7. Its Km value for L-arginine was 0.3 mM, which is about 30 times lower than that of bovine liver arginase. It was stable and active under culture conditions. When added into cultures, the arginine deiminase inhibited the growth of various human cancer cell lines at a dose of 5 ng/ml or higher by depleting L-arginine in the culture media. This effective dose was about 1000 times lower than that of bovine liver arginase. These results suggested the possibility of chemotherapeutic use of arginine deiminase for human cancers.

Potent growth inhibition of human tumor cells in culture by arginine deiminase purified from a culture medium of a Mycoplasma-infected cell line.

Two kinds of growth-inhibitory substances were found in culture of a Rous ***sarcoma*** virus-transformed rat liver cell line, RSV-BRL. The two substances were purified from the serum-free culture medium and identified as transforming growth factor beta 1 and Mycoplasma-derived arginine ***deiminase*** (EC 3.5.3.6), respectively. The ***arginine*** deiminase was an acid-labile but dithiothreitol-resistant protein with a molecular weight of 45,000...

... liver arginase. It was stable and active under culture conditions. When added into cultures, the arginine deiminase inhibited the growth of various human cancer cell lines at a dose of 5 ng...

... than that of bovine liver arginase. These results suggested the possibility of chemotherapeutic use of arginine deiminase for human cancers.

...; Sequence Data; Molecular Weight; Mycoplasma--enzymology--EN; Rats; Research Support, Non-U.S. Gov't; ***Sarcoma*** Viruses, Avian--genetics --GE; Tumor Cells, Cultured--drug effects--DE

Enzyme No.: EC 3. (Hydrolases); EC 3.5.3.6 (***arginine*** deiminase)

Chemical Name: Amino Acids; Hydrolases; arginine deiminase

6/3,K,AB/7 (Item 1 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

0010083492 BIOSIS NO.: 199598551325
Anti-tumor activity of arginine deiminase from Mycoplasma arginini and its growth-inhibitory mechanism
AUTHOR: Takaku Haruo (Reprint); Matsumoto Mitsuhiro; Misawa Satoru; Miyazaki Kaoru
AUTHOR ADDRESS: Pharm. Biotechnol. Lab., Japan Energy Corp., 3-17-35 Niizo-minami, Toda, Saitama 335, Japan**Japan
JOURNAL: Japanese Journal of Cancer Research 86 (9): p840-846 1995 1995
ISSN: 0910-5050
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Two kinds of ***arginine*** ***deiminase*** (AD, EC 3.5.3.6) were purified from cell extracts of Mycoplasma arginini (a-AD) and Mycoplasma hominis (h-AD), and their enzymic properties and anti-tumor activities were compared. The a-AD enzyme strongly inhibited the growth of mouse hepatoma cell line MH134 in vitro, and its concentration required for 50% growth inhibition (IC-50) was estimated to be about 10 ng/mi. The

IC-50 value of h-AD against the same cell line was estimated to be about 100 ng/ml, due to its low enzyme activity under the physiological pH condition, i.e., pH 7.4. These results show that the reaction pH profile of the a-AD was superior to that of the h-AD as an anti-tumor enzyme. Moreover, the effects Of L-arginine metabolism-related substances on the anti-tumor activity of the a-AD were examined to study the growth-inhibitory mechanism of this enzyme. The addition of 2 or 4 MM L-arginine restored, in a dose-dependent manner, the growth of mouse MH134 hepatoma and Meth A fibrosarcoma cell lines that had been inhibited by 20 ng/ml of the a-AD. The addition of 2 or 4 MM L-ornithine, which is biosynthesized from L-arginine in the urea cycle and is the starting material in the polyamine-biosynthesis pathway, also partially restored it in a dose-dependent manner. These results indicate that the tumor cell growth inhibition caused by a-AD originates from the depletion of the essential nutrient L-arginine, and that the resulting block of the polyamine-biosynthesis pathway is involved in part in the inhibitory mechanism.

Anti-tumor activity of arginine deiminase from Mycoplasma arginini and its growth-inhibitory mechanism

ABSTRACT: Two kinds of ***arginine*** ***deiminase*** (AD, EC 3.5.3.6) were purified from cell extracts of Mycoplasma arginini (a...
...anti-tumor activities were compared. The a-AD enzyme strongly inhibited the growth of mouse hepatoma cell line MH134 in vitro, and its concentration required for 50% growth inhibition (IC-50...

...4 MM L-arginine restored, in a dose-dependent manner, the growth of mouse MH134 hepatoma and Meth A fibrosarcoma cell lines that had been inhibited by 20 ng/ml of...
...REGISTRY NUMBERS: ***ARGININE*** ***DEIMINASE*** ;
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ARGININE DEIMINASE;
MISCELLANEOUS TERMS: ... ***ARGININE*** ***DEIMINASE*** ;

6/3,K,AB/8 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

15196807 Genuine Article#: 048KP Number of References: 41
Title: Drug evaluation: ADI-PEG-20 - a PEGylated arginine deiminase for arginine-auxotrophic cancers (ABSTRACT AVAILABLE)
Author(s): Shen LJ (REPRINT) ; Shen WC
Corporate Source: Natl Taiwan Univ,Coll Med, Sch Pharm,12F 1 Ren Ai Rd,Sec 1/Taipei 100//Taiwan/ (REPRINT); Natl Taiwan Univ,Coll Med, Sch Pharm,Taipei 100//Taiwan/; Univ So Calif,Sch Pharm,Los Angeles//CA/90033(ljshen@ha.mc.ntu.edu.tw; weishen@usc.edu)
Journal: CURRENT OPINION IN MOLECULAR THERAPEUTICS, 2006, V8, N3 (JUN), P 240-248
ISSN: 1464-8431 Publication date: 20060600
Publisher: CURRENT DRUGS LTD, MIDDLESEX HOUSE, 34-42 CLEVELAND ST, LONDON W1P 6LB, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Pheonix is developing ADI-PEG-20, a PEGylated arginine deiminase for the potential treatment of hepatocellular carcinoma, for which the Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products have granted the drug Orphan Drug status, and melanoma, for which the FDA has also awarded ADI-PEG-20 Orphan Drug status. ADI-PEG-20 is also being investigated for the potential treatment of influenza virus infection

and hepatitis C virus infection.

Title: Drug evaluation: ADI-PEG-20 - a PEGylated arginine deiminase for arginine-auxotrophic cancers
Abstract: Pheonix is developing ADI-PEG-20, a PEGylated arginine deiminase for the potential treatment of hepatocellular carcinoma, for which the Food and Drug Administration (FDA...
...Identifiers--NITRIC-OXIDE SYNTHASE; MYCOPLASMA-ARGININI; HEPATOCELLULAR-CARCINOMA; ANTITUMOR-ACTIVITY; HEPATOMA-CELLS; ASPARAGINASE; MECHANISM; GROWTH; FORMULATIONS; INHIBITION

6/3,K,AB/9 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03557563 Genuine Article#: PM446 Number of References: 143
Title: AIDS-ASSOCIATED MYCOPLASMAS (Abstract Available)
Author(s): BLANCHARD A; MONTAGNIER L
Corporate Source: INST PASTEUR,DEPT AIDS & RETROVIRUSES,VIRAL ONCOL UNIT/F-75724 PARIS//FRANCE/
Journal: ANNUAL REVIEW OF MICROBIOLOGY, 1994, V48, P687-712
ISSN: 0066-4227
Language: ENGLISH Document Type: REVIEW
Abstract: Previously, we hypothesized that mycoplasmas could act as cofactors accelerating the progression of HIV disease. In the present paper, we review the. current knowledge on three mycoplasmas (Mycoplasma fermentans, M. penetrans, and M. pirum) that have been implicated as these putative cofactors. All three mycoplasmas have been isolated from patients with HIV infection, and serological studies have suggested that the presence of M. penetrans could be associated with HIV infection. These mycoplasmas share the capacity to hydrolyze arginine and ferment glucose as well as to attach to and invade eukaryotic cells. The possible mechanisms that could allow mycoplasmas to influence HIV pathogenesis, specifically through the activation of the immune system or the production of superantigen or by contributing to the oxidative stress observed in HIV-infected subjects, are discussed. These studies have offered and will continue to offer major contributions to a better understanding of mycoplasmal flora in humans and have begun to unveil some of the mechanisms of virulence of these organisms.

...Identifiers--HUMAN-IMMUNODEFICIENCY-VIRUS; FERMENTANS INCOGNITUS STRAIN; HIV-INFECTED PATIENTS; POLYMERASE CHAIN-REACTION; ARGININE DEIMINASE GENE; TUMOR-NECROSIS-FACTOR; RIBOSOMAL-RNA GENES; II MHC PROTEINS; T-CELL MITOGEN; KAPOSIS-SARCOMA
...Research Fronts: GENITAL ULCER DISEASES AMONG MALE SEXUALLY-TRANSMITTED DISEASE PATIENTS)
92-2329 001 (AIDS-ASSOCIATED KAPOSIS-SARCOMA CELLS IN CULTURE EXPRESS VASCULAR ENDOTHELIAL GROWTH-FACTOR; ORAL SUBMUCOSAL DENDROCYTES; HIV TAT GENE)

6/3,K,AB/10 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03054087 Genuine Article#: NC773 Number of References: 57
Title: REGULATION OF PUTRESCINE EXPORT IN LIPOPOLYSACCHARIDE OR IFN-GAMMA-ACTIVATED MURINE MONOCYTIC-LEUKEMIC RAW-264 CELLS (Abstract Available)
Author(s): TJANDRAWINATA RR; HAWEL L; BYUS CV
Corporate Source: UNIV CALIF RIVERSIDE,DIV BIOMED SCI/RIVERSIDE//CA/92521;

UNIV CALIF RIVERSIDE,DIV BIOMED SCI/RIVERSIDE//CA/92521; UNIV CALIF RIVERSIDE,DEPT BIOCHEM/RIVERSIDE//CA/92521
Journal: JOURNAL OF IMMUNOLOGY, 1994, V152, N6 (MAR 15), P3039-3052
ISSN: 0022-1767
Language: ENGLISH Document Type: ARTICLE
Abstract: The regulation of putrescine/polyamine export out of the cell was investigated during activation of monocytic-leukemic RAW 264 cells with LPS and IFN-gamma. The RAW 264 cells exported putrescine constitutively at a significant rate into the culture medium. This export process appeared to be selective for putrescine in that only a small amount of other polyamines (spermidine and N-1-acetylspermidine) was found in the culture medium. LPS and IFN-gamma alone and in combination markedly stimulated putrescine export and nitrite production throughout a 24-h period. The efflux of putrescine but not nitrite was further increased by the addition of ornithine (the amino acid precursor of putrescine) to the culture medium. LPS and ornithine also stimulated the intracellular accumulation of putrescine in primary inflammatory macrophages and the export of putrescine into the peritoneal exudate of the mouse. A detailed comparison of the steady state rates of accumulation of intracellular putrescine/polyamines and the rate of putrescine efflux from the cells constitutively and after LPS, IFN-gamma, and ornithine indicated that a surprisingly large fraction of total polyamine biosynthesis is comprised of exported putrescine. The observed dose-dependent inhibition of putrescine export with the drug verapamil implicated the involvement of a specific membrane transport system sensitive to calcium influx in this process. The data are discussed in regard to the potential involvement of putrescine export in the regulation of intracellular polyamine levels, cell differentiation, and macrophage-mediated cytotoxicity.

...Identifiers--SPERMINE N1-ACETYLTRANSFERASE ACTIVITY; ORNITHINE DECARBOXYLASE ACTIVITY; L-ARGININE DEIMINASE; HAMSTER OVARY CELLS; POLYAMINE ACETYLATION; LIQUID-CHROMATOGRAPHY; HEPATOMA -CELLS; AMINO-ACIDS; EXCRETION; LINES
...Research Fronts: P388/VCR LEUKEMIA MODEL)
92-7742 001 (POLYAMINE OXIDASE; SPERMIDINE NUCLEAR ACETYLATION; LOGARITHMICALLY GROWING RAT HEPATOMA-CELLS)

6/3,K,AB/11 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10890986 IFI Acc No: 2005-0129706
IFI Publication Control No: 2005-0129706 IFI Chemical Acc No: 2005-0029740
Document Type: C
MODIFIED ARGININE DEIMINASE
Inventors: Clark Mike A (US)
Assignee: Phoenix Pharmacologics Inc
Assignee Code: 56130
Attorney, Agent or Firm: WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE, 46TH FLOOR, 1650 MARKET STREET, PHILADELPHIA, PA, 19103, US
Publication (No,Kind,Date), Applic (No,Date):
US 20050129706 A1 20050616 US 2004757843 20040115
Cont.-in-part Pub(No),Applic(No,Date): US 6183738 US 9823809 19980213
Division Pub(No),Applic(No,Date): US 6737259 US 2000723546 20001128
Priority Applic(No,Date): US 2004757843 20040115; US 9823809 19980213; US 2000723546 20001128
Provisional Applic(No,Date): US 60-46200 19970512

Abstract: The present invention is directed to arginine

deiminase modified with polyethylene glycol, to methods of treating cancer, and to methods of treating and/or inhibiting metastasis.

MODIFIED ARGININE DEIMINASE

Abstract: The present invention is directed to arginine deiminase modified with polyethylene glycol, to methods of treating cancer, and to methods of treating and...

Exemplary Claim:
...N G

1-22. (canceled)
23. A method of enhancing the circulating half life of ***arginine*** deiminase comprising modifying said arginine deiminase by covalently bonding said arginine deiminase via a linking group to polyethylene glycol, wherein the arginine deiminase is derived from a microorganism of the genus selected from the group consisting of: Steptococcus...

Non-exemplary Claims:
24. A method of enhancing the tumoricidal activity of ***arginine*** deiminase comprising modifying said arginine deiminase by covalently bonding said arginine deiminase via a linking group to polyethylene glycol, wherein the arginine deiminase is derived from a microorganism of the genus selected from the group consisting of: Steptococcus...

...of treating a tumor in a patient comprising administering to said patient a compound comprising arginine deiminase covalently bonded via a linking group to polyethylene glycol, wherein the arginine deiminase is derived from a microorganism of the genus selected from the group consisting of: Steptococcus...

...30. The method of claim 25, wherein said tumor is a ***hepatoma*** .
...

...34. The method of claim 25, wherein said tumor is a ***sarcoma*** .
...

...treating and inhibiting metastases in a patient comprising administering to said patient a compound comprising arginine deiminase covalently bonded via a linking group to polyethylene glycol, wherein the arginine deiminase is derived from a microorganism of the genus selected from the group consisting of: Steptococcus

6/3,K,AB/12 (Item 2 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10624379
IFI Chemical Acc No: 2004-0037834
Document Type: C
METHODS FOR INHIBITING VIRAL REPLICATION IN VIVO; NISTERING ARGININE DEIMINASE MODIFIED WITH POLYOXYETHYLENE GLYCOL; ANTICANCER AGENTS
Inventors: Clark Mike (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Probable Assignee (A1): Phoenix Pharmacologics Inc
Attorney, Agent or Firm: COZEN O'CONNOR, P.C., 1900 MARKET STREET, PHILADELPHIA, PA, 19103-3508, US
Publication (No,Kind,Date), Applic (No,Date):

US 20040131604 A1 20040708 US 2003674666 20030929
Priority Applic(No,Date): US 2003674666 20030929
Provisional Applic(No,Date): US 60-427497 20021118

Abstract: The present invention is directed to methods of modulating viral replication in vivo comprising administering to an individual a therapeutically or prophylactically effective amount of a composition comprising arginine deiminase modified with polyethylene glycol, to methods of concurrently modulating viral replication and treating cancer, and to methods of modulating nitric oxide levels in a patient, among others.

...NISTERING ***ARGININE*** ***DEIMINASE*** MODIFIED WITH POLYOXYETHYLENE GLYCOL; ANTICANCER AGENTS

Abstract: ...comprising administering to an individual a therapeutically or prophylactically effective amount of a composition comprising arginine deiminase modified with polyethylene glycol, to methods of concurrently modulating viral replication and treating cancer, and...

Exemplary Claim:

...or more viruses in an individual comprising administering to said individual a composition comprising an arginine deiminase bonded to polyethylene glycol in an amount effective to inhibit viral replication in said individual.

Non-exemplary Claims:

...6. The method of claim 1 wherein said composition comprising an arginine deiminase bonded to polyethylene glycol is effective at a concentration of less than about 1 mM...

...7. The method of claim 1 wherein the amount of ***arginine*** deiminase bonded to polyethylene glycol effective to inhibit viral replication is between about 40 IU/m2...

...8. The method of claim 1 wherein the amount of ***arginine*** deiminase bonded to polyethylene glycol effective to inhibit viral replication is about 160 IU/m2 per...

...9. The method of claim 1 wherein the amount of ***arginine*** deiminase bonded to polyethylene glycol effective to inhibit viral replication lowers plasma arginine levels to less...

...10. The method of claim 1 wherein the ***arginine*** ***deiminase*** is covalently bonded via a linking group to polyethylene glycol, wherein each of said polyethylene...

...claim 1 wherein from about 7 to about 15 polyethylene glycol molecules are bonded to ***arginine*** ***deiminase*** .

...

...1 wherein from about 9 to about 12 said polyethylene glycol molecules are bonded to ***arginine*** ***deiminase*** .

...

...16. The method of claim 1 wherein said ***arginine*** ***deiminase*** is derived from a microorganism of the genus Mycoplasma...

...18. The method of claim 1 wherein the ***arginine*** ***deiminase*** has an amino acid sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6...

...19. The method of claim 1 wherein the ***arginine*** ***deiminase*** has an amino acid sequence of SEQ ID NO: 1 or 4...

...comprising the step of administering to said individual an amount of a composition comprising an arginine deiminase bonded to polyethylene glycol effective to inhibit viral replication in said individual...

...or more viruses comprising administering to said individual an amount of a composition comprising an arginine deiminase bonded to polyethylene glycol effective to inhibit viral replication in said individual...

...or more viruses comprising administering to said individual an amount of a composition comprising an arginine deiminase bonded to polyethylene glycol effective to inhibit viral replication in said individual...

...comprising the step of administering a therapeutically or prophylactically effective amount of a composition comprising arginine deiminase covalently bonded via a linking group to polyethylene glycol to said individual effective to inhibit...

...28. The method of claim 26 wherein the tumor is melanoma, ***sarcoma*** , or ***hepatoma*** .

...

...method for modulating nitric oxide levels in an individual comprising administering an amount of an arginine deiminase bonded to polyethylene glycol effective to modulate nitric oxide to said individual...

...34. The method of claim 33 wherein the ***arginine*** ***deiminase*** is covalently bonded via a linking group to polyethylene glycol, wherein each of said polyethylene...

...claim 34 wherein from about 7 to about 12 polyethylene glycol molecules are bonded to ***arginine*** ***deiminase*** .

...

...38. The method of claim 33 wherein said ***arginine*** ***deiminase*** is derived from a microorganism of the genus Mycoplasma...

...arginine comprising: (a) contacting a sample comprising one or more viruses with a composition comprising arginine deiminase bonded to polyethylene glycol; and (b) comparing levels of viral replication in the presence and absence of the composition comprising arginine deiminase bonded to polyethylene glycol; wherein decreased viral replication in samples contacted with arginine deiminase is indicative of viral sensitivity to arginine ***deiminase*** .

...

...oxide comprising: (a) contacting a sample comprising one or more viruses with a composition comprising arginine deiminase bonded to polyethylene glycol; and (b) comparing levels of viral replication in the presence and absence of the composition comprising arginine deiminase bonded to polyethylene glycol, wherein decreased viral replication in samples contacted with arginine deiminase is indicative of viral sensitivity to nitric oxide...

...said compound is administered to said individual simultaneously with the administration of said composition comprising arginine ***deiminase*** bonded to polyethylene glycol...

...need thereof comprising administering a therapeutically or

prophylactically effective amount of a composition comprising an arginine deiminase bonded to polyethylene glycol to said individual...

...liver function in an individual comprising administering a therapeutically effective amount of a composition comprising arginine deiminase bonded to polyethylene glycol to said individual...

...44 wherein the liver function of said individual prior to administration of the composition comprising arginine deiminase bonded to polyethylene glycol is Child-Pugh level A...

...44 wherein the liver function of said individual prior to administration of the composition comprising arginine deiminase bonded to polyethylene glycol is Child-Pugh level B...

...44 wherein the liver function of said individual prior to administration of the composition comprising arginine deiminase bonded to polyethylene glycol is Child-Pugh level C...

...the individual; and b) comparing viral replication in the sample contacted with a composition comprising arginine deiminase bonded to polyethylene glycol under conditions suitable for viral replication to viral replication in the sample in the absence of a composition comprising arginine deiminase bonded to polyethylene glycol, wherein an inhibition of viral replication of at least 40% in

6/3,K,AB/13 (Item 3 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 3967718 IFI Acc No: 0041696
IFI Publication Control No: 0041696
Document Type: C
(A1) YEAST EXPRESSION SYSTEMS, METHODS OF PRODUCING POLYPEPTIDES IN YEAST, AND COMPOSITIONS RELATING TO SAME; GENETIC ENGINEERING; FOR PRODUCTION OF ENZYMES, GROWTH FACTORS, CYTOKINES, IMMUNOGENIC PROTEINS, AND IMMUNOGLOBULIN PROTEINS
(B2) YEAST EXPRESSION SYSTEMS, METHODS OF PRODUCING POLYPEPTIDES IN YEAST, AND COMPOSITIONS RELATING TO SAME; GENETIC ENGINEERING; FOR PRODUCTION OF ENZYMES, GROWTH FACTORS, CYTOKINES, IMMUNOGENIC PROTEINS, AND IMMUNOGLOBULIN PROTEINS
Inventors: Clark Mike A (US)
Assignee: (A1) Unassigned Or Assigned To Individual
(B2) Phoenix Pharmacologics Inc
Assignee Code: (A1) 68000; (B2) 56130
Probable Assignee (A1): Phoenix Pharmacologics Inc
Attorney, Agent or Firm: Woodcock Washburn LLP
Publication (No,Kind,Date), Applic (No,Date):
US 20030092099 A1 20030515 US 2001915815 20010726
US 6645739 B2 20031111 US 2001915815 20010726
Calculated Expiration: 20210726
Notes: INDEXED FROM APPLICATION
Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 20051108
Prior Publication(No,Date),Applic(No,Date):US 20030092099 A1 20030515
Priority Applic(No,Date): US 2001915815 20010726

Abstract: (US 20030092099 A1)
The present invention provides novel expression systems for producing

desired polypeptides in certain strains of yeast. The present invention further provides methods for producing polypeptide products using such expression systems. The present invention also provides compositions relating to the same.

Abstract: (US 6645739 B)
The present invention provides novel expression systems for producing desired polypeptides in certain strains of yeast. The present invention further provides methods for producing polypeptide products using such expression systems. The present invention also provides compositions relating to the same.

Non-exemplary Claims:
...immunodeficiency virus promoter, maloney virus promoter, cytomegalovirus immediate early promoter, Epstein Barr virus promoter, rous sarcoma virus promoter, human actin promoter, human myosin promoter, human hemoglobin promoter, human muscle creatine promoter...

...12. The expression system of claim 11 wherein the ***deiminase*** is ***arginine*** ***deiminase*** .
...

...immunodeficiency virus promoter, maloney virus promoter, cytomegalovirus immediate early promoter, Epstein Barr virus promoter, rous sarcoma virus promoter, human actin promoter, human myosin promoter, human hemoglobin promoter, human muscle creatine promoter...

...9. The expression system of claim 8 wherein the ***deiminase*** is ***arginine*** ***deiminase*** .

6/3,K,AB/14 (Item 4 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 3457265 IFI Acc No: 0104399
IFI Publication Control No: 0104399
Document Type: C
MODIFIED ARGININE DEIMINASE; COVALENTLY BONDED TO POLYOXYETHYLENE GLYCOL VIA SUCCINIMIDE-TYPE LINKER; ANTITUMOR, ANTICARCINOGENIC, AND ANTIMETASTASIS AGENTS
Inventors: Clark Mike A (US)
Assignee: Phoenix Pharmacologics Inc
Assignee Code: 56130
Attorney, Agent or Firm: Woodcock Washburn Kurtz Mackiewicz & Norris LLP
Publication (No,Kind,Date), Applic (No,Date):
US 6183738 B1 20010206 US 9823809 19980213
Calculated Expiration: 20180213
Document Type: REISSUE REQUESTED
Priority Applic(No,Date): US 9823809 19980213

Abstract: The present invention is directed to arginine deiminase modified with polyethylene glycol, to methods of treating cancer, and to methods of treating and/or inhibiting metastasis.

MODIFIED ARGININE DEIMINASE;

Abstract: The present invention is directed to arginine deiminase modified with polyethylene glycol, to methods of treating cancer, and to methods of treating and...

Exemplary Claim:

D R A W I N G

1. A compound comprising ***arginine*** ***deiminase*** covalently bonded via a linking group to polyethylene glycol, wherein the polyethylene glycol has a...

Non-exemplary Claims:

...5. The compound of claim 1, wherein said ***arginine*** ***deiminase*** is derived from a microorganism of the genus Mycoplasma...

...7. The compound of claim 1, wherein said ***arginine*** ***deiminase*** is covalently bonded to about 7 to about 15 polyethylene glycol molecules...

...8. The compound of claim 7, wherein said ***arginine*** ***deiminase*** is covalently bonded to about 9 to about 12 polyethylene glycol molecules...

...15. The method of claim 10, wherein said tumor is a ***hepatoma*** .
...

...19. The method of claim 10, wherein said tumor is a ***sarcoma*** .
...

...21. A method of enhancing the circulating half life of ***arginine*** deiminase comprising modifying said arginine deiminase by covalently bonding said arginine deiminase via a linking group to polyethylene glycol, wherein the polyethylene glycol has a total weight...

...22. A method of enhancing the tumoricidal activity of ***arginine*** deiminase comprising modifying said arginine deiminase by covalently bonding said arginine deiminase via a linking group to polyethylene glycol, wherein the polyethylene glycol has a total weight

?